

INNOVATIONS

in Neurosciences



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University Hospitals Case Medical Center and Case Western Reserve University School of Medicine are consistently recognized as two of the premier institutions in the nation, according to U.S. News & World Report's annual rankings.

Message from the Directors

A Tradition of Quality



The passage of health care reform legislation is changing the way care is delivered, bringing a new focus to optimizing the quality of patient care while controlling costs and using resources efficiently. At University Hospitals Neurological Institute, the emphasis on quality is not an outgrowth of new health care legislation, but an integral part of our patient care tradition. The UH Neurological Institute has always coupled innovation with a philosophy of continuous improvement in quality of care and patient outcomes.

This issue of Innovations in Neurosciences explores some of the innovative ways in which we utilize technology, research and collaboration to deliver exceptional care that achieves the best possible outcomes for our patients:

- The Neurological Outcomes Center, one of the first centers of its kind in the United States, is drawing on the expertise, empathy and resources in the community to help educate and empower stroke and Parkinson's disease patients to self-manage and adhere to their treatment plans.
- A remarkable confluence of simulation technology and neurosurgical expertise, the Surgery Rehearsal Platform was developed through a collaboration between ex-Israeli Air Force officers and UH Case Medical Center physicians. Designed to help doctors rehearse complex procedures using medical images of actual patients,

Warren R. Selman, MD
Director, UH Neurological Institute
Neurosurgeon-in-Chief, University Hospitals
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the platform will be evaluated at selected neurosurgery centers across the United States to determine if it improves surgeons' efficiency and reduces patient time in the OR.

■ At the forefront of epilepsy research is a new method of treatment that uses deep brain stimulation of the fornix in patients with intractable mesial temporal lobe epilepsy. Now in phase 1 testing, this novel treatment approach shows great promise for decreasing seizures while preserving or improving memory in these patients, who otherwise face poor health outcomes and quality of life.

■ In collaboration with pediatric epileptologists at UH Rainbow Babies & Children's Hospital, our epilepsy surgery team successfully performed a temporoparietooccipital disconnection with amygdalo hippocampectomy in a 10-month-old male with a rare form of intractable epilepsy.

Lastly, we are proud to announce that UH Case Medical Center has received the 2012 American Hospital Association-McKesson Quest for Quality Prize. The prestigious award named UH Case Medical Center the top hospital in the nation for its leadership and innovation in quality improvement and safety.

Please visit UHhospitals.org to learn more about our services, which are available throughout northeast Ohio to serve you and your patients.

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The commitment to exceptional patient care begins with revolutionary discovery. University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a national leader in medical research and education and consistently ranked among the top research medical schools in the country by U.S. News & World Report. Through their faculty appointments at Case Western Reserve University School of Medicine, physicians at UH Case Medical Center are advancing medical care through innovative research and discovery that bring the latest treatment options to patients.

Curing an Infant's Continuous Seizures

An innovative brain surgery disconnects epileptic tissue



Jonathan Miller, MD, Director, Functional and Restorative Neurosurgery, UH Neurological Institute; and Assistant Professor, Neurological Surgery, Case Western Reserve University School of Medicine

Neurosurgeons at University Hospitals Neurological Institute recently performed successful brain surgery on a 10-month-old infant by separating the region of the brain responsible for seizure onset from the surrounding healthy brain, immediately stopping the infant's seizures. Temporoparietooccipital (TPO) disconnection is a novel operation that offers lower risk of complications and quicker recovery, and yields superior long-term results compared with traditional methods that involve removing large, seizure-causing areas of the brain. TPO disconnection has not been previously reported to have been performed in the U.S.

Jonathan Miller, MD, Director, Functional and Restorative Neurosurgery, UH Neurological Institute; and Assistant Professor, Neurological Surgery, Case Western Reserve University School of Medicine, performed the operation on the boy, who had been diagnosed with intractable epilepsy at two weeks of age. The infant had started seizing uncontrollably and continued with multiple daily seizures that increasingly affected his ability to develop normally. The seizures continued despite a number of antiseizure medications prescribed by his primary neurologist, **Mark Scher, MD**, Chief, Division of Pediatric Neurology, University Hospitals Rainbow Babies & Children's Hospital; and Professor, Pediatrics, Case Western Reserve University School of Medicine.

The infant was referred early for a presurgical evaluation to **Asim Shahid, MD**, pediatric epileptologist, Division of Pediatric Epilepsy, UH Rainbow Babies & Children's Hospital; and Assistant Professor, Pediatrics, Case Western Reserve University School of Medicine. Dr. Shahid and the team of pediatric epilepsy experts, including **Ingrid Tuxhorn, MD**, Chief, Division of Pediatric Epilepsy, UH Rainbow Babies & Children's Hospital and UH Neurological Institute; and Professor, Pediatrics, Case Western Reserve University School of Medicine, determined that the child was a suitable surgical candidate.

"The accuracy of diagnosis in these young children rests on our expertise in using leading-edge imaging and video technology and the experience of the epileptologist," Dr. Tuxhorn says. "Sometimes, there is a tipping point where the whole EEG is very abnormal and the child is at an extremely high risk for developmental delays that can never be regained. There was a two- to three-month window in this and other similar cases that compelled us to move forward with the early surgery rather than wait any longer."

The case involved cooperation among the pediatric neurologist, epileptologist and neurosurgeon. "The fact that the child was referred to the experts very early

enabled us to have everyone on board so we could optimally time the surgery and cure this child," Dr. Tuxhorn says.

TPO disconnection is the treatment of choice for infants and children with refractory epilepsy and posterior quadrant epileptogenic lesions. "With TPO disconnection, we are able to keep most of the brain intact, which can effectively treat the seizures without the complications often seen when a large amount of brain tissue is resected," Dr. Miller says. Early diagnosis and treatment of pediatric epilepsy is very important since recurrent seizures have drastic effects on early brain development. Also, during early infancy, plasticity allows healthy brain tissue to take over functions that normally would have developed in diseased tissue. An average of two to three pediatric epilepsy surgeries are performed every month at UH Rainbow Babies & Children's Hospital and the epilepsy surgery program is planning to perform 20-25 surgeries in 2012, making it the second largest program in Northeast Ohio.

The ability of UH Rainbow Babies & Children's Hospital's Division of Pediatric Epilepsy and UH Neurological Institute to perform such complex surgeries is the result of their transdisciplinary nature, which brings together a variety of disciplines. The Division of Pediatric Epilepsy, under the leadership of Dr. Tuxhorn, consists of an interdisciplinary team of experts offering specialized medical and surgical treatments for the full range of seizure disorders. As a Comprehensive Level IV pediatric epilepsy center, the division serves as a regional, national and international center of excellence.

UH Rainbow Babies & Children's Hospital's pediatric clinical neurological sciences, together with UH Neurological Institute, offers a complete evaluation for epilepsy surgery to diagnose and localize complex seizure disorders and plan treatment. Interdisciplinary collaboration across various departments and institutes means experts from across disciplines create the best possible patient management plans.

"UH Rainbow Babies & Children's Hospital is proud to be at the forefront of implementing innovative treatment plans that provide the best possible outcomes for patients," says **Warren Selman, MD**, Interim Chief, Pediatric Neurosurgery, UH Rainbow Babies & Children's Hospital; UH Neurological Institute Director and Neurosurgeon-in-Chief, University Hospitals; and the Harvey Huntington Brown Jr., Professor and Chair, Department of Neurological Surgery, Case Western Reserve University School of Medicine.

For more information on this surgical procedure, contact Dr. Miller at JonathanMiller@UHhospitals.org.

Pre-Living the Future

A surgical simulator uses patient-specific data to help neurosurgeons rehearse complex procedures



Warren R. Selman, MD, Director, UH Neurological Institute; Neurosurgeon-in-Chief, University Hospitals; Harvey Huntington Brown Jr. Professor and Chair, Department of Neurological Surgery, Case Western Reserve University School of Medicine

What can surgeons learn from the experience of military fighter pilots?

Plenty, it turns out. A chance encounter in 2009 at a coffee shop between University Hospitals' Neurosurgeon-in-Chief and two former Israeli Air Force officers led to a collaboration that may transform the way surgeons prepare for and perform complex procedures. The product of that teamwork is a surgical simulator that uses the same technology as flight simulators to allow realistic, interactive run-throughs of brain surgeries prior to actual procedures.

The former officers, Moty Avisar and Alon Geri, were working in Northeast Ohio with Lockheed Martin. In the coffee shop, "I overheard them talking about flight simulators," says **Warren R. Selman, MD**, Director, UH Neurological Institute; Neurosurgeon-in-Chief, University Hospitals; Harvey Huntington Brown Jr. Professor and Chair, Department of Neurological Surgery, Case Western Reserve University School of Medicine. "I'd been thinking about that in the past, about how we don't really rehearse the way they do for dangerous flight missions. It led to a conversation about whether we could do this for surgery, and subsequently we found out we could."

Patient-Specific Images

Just as flight simulators use terrain satellite imageries and other information obtained from drone flights over a targeted area, the Selman Surgery Rehearsal Platform (SRP) utilizes two-dimensional images from a specific patient's CT scans, MRIs and angiograms. It then creates a dynamic, interactive, three-dimensional environment that allows surgeons to see and feel what they will experience during the actual procedure. Using the same tools he or she would use in the operation, the surgeon views and interacts with the images on the simulator's screen.

The SRP breaks new ground in two respects, Dr. Selman says. First, unlike the simulators now on the market, the SRP was designed to simulate complex, open surgical procedures. In addition, other simulators do not use patient-specific images to create the surgical environment. "There's a big difference in simulators between those that just allow you to train in general on somebody else's images, and those that actually simulate the environment that you're going to see tomorrow," Dr. Selman points out. "With the SRP, you're pre-living the future, as they say to the pilots."

Initially, Surgical Theater LLC, the corporation



formed by the former Israeli officers, is offering its product that simulates brain aneurysm surgeries, one of the most complex neurosurgical procedures, according to Dr. Selman. Eventually, the SRP will be used to help surgeons rehearse for other complex operations, including the removal of skull-based tumors. "Microsurgical excision of a meningioma or acoustic neuroma located at the base of the skull adjacent to the brainstem, cranial nerves and vital arterial supply can be quite a technical challenge if you don't do a lot of them, or even if you do," Dr. Selman says.

The SRP may turn out to be as valuable to experienced surgeons as it is to residents and other trainees, Dr. Selman notes, because "even though Tiger Woods has probably swung the golf club a bazillion times, he still goes out to the practice range both before and after a tournament. So even for an experienced surgeon, this type of practice is very important. The simulator takes learning or practice out of the OR environment and puts it in a safe environment."

One recent achievement for the team is development of an OR version of the SRP. This "OR Suite" will allow surgeons to review the prepared surgery plan in the OR and to "warm up" before performing each surgery phase.



1: From left, Warren R. Selman, MD, with former Israeli Air Force officers Moty Avisar, President, Surgical Theater, and Alon Geri, Vice President of Engineering, Surgical Theater.

2: Dr. Selman guides one of the controllers of the Surgery Rehearsal Platform during an interactive run-through prior to an actual procedure.

3: An actual microscopic view of an aneurysm as seen by the surgeon using the Surgery Rehearsal Platform.

Aside from the ability to execute the surgery based on the surgery plan, the OR Suite was tailor-made for the OR requirements, Dr. Selman says.

For example, a unique feature of the OR Suite is a “hands-free” interface, similar to high-end video games – the surgeon does not touch any instrument to operate the device. This is a major advantage over today’s technology, which requires surgeons to use a mouse or a keyboard to review CT or MRI images in the OR, forcing them to then resterilize their hands. This may happen a few times during the surgery. The OR Suite’s hands-free features will improve OR effectiveness by providing an efficient way to link the surgery plan to the surgery itself and by eliminating the need to sterilize after each review of the CT or MRI images.

Measuring Success

Surgical Theater is poised to seek a 510(k) clearance from the Food and Drug Administration, which will allow it to market the SRP for commercial use. In order to provide evidence for the SRP’s clinical value proposition and improvement of outcome, Dr. Selman plans to collaborate with colleagues throughout the country, many of whom are chairmen of major academic neurosurgery

programs. “What we are planning to do in the clinical trial is to provide evidence for improved effectiveness,” he says. “For example, how many times you put on a clip, reposition a clip or change something. If you can decrease those, you will decrease your overall OR time and the likelihood that you’re going to hurt something. Those types of things can be measured, and that’s what we’re going to be looking at.”

In the near future, the SRP will be expanded to other brain and spine procedures, and ultimately to surgeries in other disciplines as well, Dr. Selman says. He envisions that surgeons may one day view it as they now regard surgical navigation. “We call it an addiction factor. When I first started training, we never used a surgical navigation device – we felt that’s what a good surgeon knows how to do,” he says. “But now, among the younger trainees and even myself, I admit that it’s one of the things I can’t imagine living without. We feel it will prove the same with the SRP. It’s very exciting, and I’m pleased to be a part of it.”

Dr. Selman is a consultant to and holds an equity option with Surgical Theater LLC.

Research Connection

Finding a New Approach to Epilepsy Treatment

Neurologist targets white matter with low-frequency DBS



Mohamad Koubeissi, MD, University Hospitals Case Medical Center; and Assistant Professor, Neurology, Case Western Reserve University School of Medicine



Hans Lüders, MD, PhD, University Hospitals Case Medical Center; and Professor, Neurology, Case Western Reserve University School of Medicine



Dominique M. Durand, PhD, Elmer Lincoln Lindseth Professor in Biomedical Engineering, Case School of Engineering, Case Western Reserve University

A unique method of treatment using deep brain stimulation (DBS) could offer new hope to patients with intractable mesial temporal lobe epilepsy, a group that now is generally faced with poor health outcomes and quality of life. A team of physicians at University Hospitals Neurological Institute's Epilepsy Center and a researcher at Case Western Reserve University will test the safety and tolerability of the new approach in 16 patients with the disorder, according to **Mohamad Koubeissi, MD**, University Hospitals Case Medical Center; and Assistant Professor, Neurology, Case Western Reserve University School of Medicine, who developed this technique with **Hans Lüders, MD, PhD**, University Hospitals Case Medical Center; and Professor, Neurology, Case Western Reserve University School of Medicine, and **Dominique M. Durand, PhD**, Elmer Lincoln Lindseth Professor in Biomedical Engineering, Case School of Engineering, Case Western Reserve University.

Although DBS is already an accepted treatment for patients with some neurologic and psychiatric disorders, its success in epilepsy has been limited. The UH team, however, will target a different area of the brain and employ new parameters for stimulation in its phase 1 trial, says Dr. Koubeissi. "Every other DBS trial that has been done to treat epilepsy has stimulated the neurons – the gray matter – of the brain," he explains. "This stimulation has been performed at very high frequencies, in the range of 100 to 130 pulses per second. In our trial, we're stimulating the fiber tract, or the white matter tract, at low frequencies."

Curing Seizures, Preserving Memory

The first line of treatment for temporal lobe epilepsy, the most common form of focal epilepsy, is antiepileptic medication. Patients who fail drug therapy and whose seizures severely impact their quality of life may be treated with resection of the temporal lobe, says Dr. Koubeissi. But because the temporal lobe contains the hippocampus, which is essential to memory function, the temporal lobe is usually not removed unless the hippocampus is already so damaged by seizures that it no longer contributes significantly to memory function.

"So, what do we do with a patient who has temporal lobe epilepsy but good memory function? We stimulate the fiber tract, the long processes of brain cells that are

covered in insulating myelin," explains Dr. Koubeissi.

"That includes fibers from the fornix as well as from the dorsal hippocampal commissure. The idea is that if we stimulate the fiber tract, we will activate the whole hippocampus and override it in a manner that prevents the generation of epileptiform discharges and decrease seizures. This is the hypothesis."

The second innovation, stimulation at low frequencies rather than high, stems from a hope of preserving or even improving memory function. "Low frequency stimulation can induce plastic changes in the target tissue, and activate the whole limbic circuit, which is important for emotions and memory," Dr. Koubeissi notes. "Verbal memory, the recollection of facts and names and language, is the type that we are seeking to salvage from this project."

Seeking Optimal Stimulation

Preliminary data from human studies, as well as animal studies at Case Western Reserve University, show proof of principle for targeting the fiber tract and using low-frequency stimulation, Dr. Koubeissi says, so the next step is to determine what current intensity is safest. Participants in the trial will be randomized to receive stimulation at a frequency of either 1 Hz or 5 Hz, and the current intensity will initially be 2 mA. Two months of regular stimulation (four hours on, four hours off) will be followed by another two months of no stimulation, which will allow any carryover effects of the initial stimulation to wear off. Dr. Koubeissi plans to increase it by 2 mA for subsequent two-month blocks and continue the process for one year.

"In a secondary analysis, we'll look to make sure this treatment improves the seizures," he notes. "Once we've established what kind of intensity and what frequency has the best combination of no side effects with efficacy against seizures, we'll apply for a phase 3 clinical trial to test a larger number of patients in multiple centers."

Ask Our Expert

For more information about treatment of temporal lobe epilepsy using DBS, contact Hans Lüders, MD, PhD, at **Hans.Luders@UHhospitals.org**.

Effective Health Promotion

The Neurological Outcomes Center focuses on making interventions more effective



Martha Sajatovic, MD, Professor, Psychiatry and Neurology, and the Willard Brown Chair in Neurological Outcomes Research, Case Western Reserve University School of Medicine

A broad, inclusive approach to improving patient outcomes is leading investigators at the University Hospitals Neurological Institute's Neurological Outcomes Center to look beyond the walls of the institution. Devoted exclusively to studying outcomes and quality improvements in the care for patients with neurological disorders, the three-year-old Neurological Outcomes Center is developing a reputation for novel methods of looking at neurological outcomes and for its approaches to health promotion, according to its director, **Martha Sajatovic, MD.**

"Enhancing treatment adherence and helping individual patients self-manage whatever kind of illness they have are major themes underlying our research," says Dr. Sajatovic, Professor, Psychiatry and Neurology, and the Willard Brown Chair in Neurological Outcomes Research, Case Western Reserve University School of Medicine. "Health care is a partnership between patient and clinician, occurring within the context of family and society. It's everybody's job."

The Neurological Outcomes Center received more than \$3.2 million in funding in just the first half of 2012 and has more than two dozen projects under way or in development.

Enlisting the Aid of Peers

A two-year study funded by a grant from the National Institutes of Health demonstrates how the Neurological Outcomes Center seeks to take advantage of strengths in families and communities in helping patients improve their own health. All National Institutes of Health funding for basic and clinical research is awarded to the School of Medicine at Case Western Reserve University. The Targeted Management Intervention for African-American Men with Transient Ischemic Attack (TIA) or Stroke study (TEAM) focuses on African-American men ages 21 to 65 who have experienced a first-time stroke or TIA. African-Americans have a stroke rate nearly double that of the general American population, and African-Americans who experience a first stroke are younger, have greater disability, more complications and slower recovery, says Dr. Sajatovic.

"We will enroll 38 people for whom the first event hasn't caused a big deficit, but is definitely a wake-up call," she explains. Individuals who have a stroke or TIA are at significant risk for another stroke, but "hopefully, they will be able to change their future."

In the first phase of the study, researchers will assemble a Community Advisory board that includes African-American men who have suffered a stroke or TIA and their care partners. "We really need to understand what are the social and environmental factors these individuals are

dealing with, such as smoking, diet and exercise," says Dr. Sajatovic. "We'll try to get a little better handle on barriers and facilitators to recovery and health management."

The advisory board will assist in refining the intervention for the second phase of the trial, estimated to begin in spring 2013. The intervention will consist of several group sessions led by a nurse and a Peer-Care Partner dyad similar to those on the advisory board. Study participants will be randomly assigned to either the TEAM intervention or care as usual.

Treatment for Parkinson's Disease and Depression

Peer Educators also play a key role in the Neurological Outcomes Center's EXCEED (Enhanced Exercise Therapy for Patients with Parkinson's Disease) project, a pilot study funded by the Spitz Brain Health Innovation Fund and being conducted with **Benjamin Walter, MD**, Director, Deep Brain Stimulation Program, UH Neurological Institute Movement Disorders Center; and Assistant Professor, Neurology, Case Western Reserve School of Medicine. EXCEED is testing an intervention designed to improve health outcomes in individuals with Parkinson's disease and depression, which afflicts about half of Parkinson's patients, Dr. Sajatovic says.

Working with Angela Ridgel, PhD, from Kent State University, the study team will test an intervention that "combines evidence-based exercise that we know improves outcomes as well as behavioral self-management techniques to empower patients to manage their Parkinson's. We have evidence that this approach can actually improve depression. Again, we'll be using Peer Educators to help us implement the intervention." The EXCEED study team also includes Christina Whitney, PhD, ACNS-BC; Smyth; Tatsuoaka; David Riley, MD, Professor, Neurology, Case Western Reserve University School of Medicine; Steven Gunzler, MD, Assistant Professor, Neurology, Case Western Reserve University School of Medicine; and Ellen Walter, RN, CNP.

If proved effective, the interventions in both the TEAM and EXCEED projects will be standardized in a detailed manual, then tested and implemented more broadly, Dr. Sajatovic says. "We want this to be practical, something that could easily be used in other centers," she notes. "Our goal is to help advance care for patients and families dealing with Parkinson's disease."

Learn More

For more information about the Neurological Outcomes Center, please contact Elisabeth Welter at 216-368-3032.



A Pioneering Project

Drug development takes an innovative leap forward with the University Hospitals Case Medical Center Harrington Discovery Institute

Last February, University Hospitals announced a \$250 million initiative, The Harrington Project for Discovery & Development, which promises to dramatically change how drugs will advance from laboratory discoveries to commercialization, giving patients greater access to advanced treatments and cures.

The project includes a new model dedicated to physician-scientists, University Hospitals Harrington Discovery Institute, and a new mission-aligned, for-profit development company, BioMotiv. Aligning the entities will, for the first time at an academic medical center, provide a comprehensive model to accelerate discoveries and create novel therapies for the benefit of individuals and communities around the world.

The UH Harrington Discovery Institute will provide funding, mentoring and an infrastructure to advance breakthrough, patient-inspired clinical research projects. By supporting a physician-scientist led culture change that promotes drug discovery and development, the UH Harrington Discovery Institute will inspire the next generation of physician-scientists to find a home in medicine and positively impact human health.

The open design of the institute – based at UH Case Medical Center in Cleveland's University Circle – will allow for collaboration with major academic medical centers across the country. UH Case Medical Center is a nationally recognized academic medical center and is the primary affiliate of Case Western Reserve University School of Medicine.

To learn more about the UH Harrington Discovery Institute, please visit UHharringtondiscoveryinstitute.org.

University Hospitals Neurological Institute

At convenient locations throughout Northern Ohio, University Hospitals Neurological Institute delivers innovative, integrated and individualized care to patients with diseases affecting the nervous system.

Our multidisciplinary team of neurosurgeons and neurological specialists provides a full spectrum of services, including diagnosis and treatment of brain tumors, epilepsy, strokes, spine and pain disorders, Parkinson's, Alzheimer's and more. Nationally recognized experts in neurology, neurosurgery, neuroradiology and other specialties collaborate to devise personalized care plans using the latest clinical advances and leading-edge technologies.

University Hospitals Case Medical Center's Neurology and Neurosurgery Departments have once again been named one of the nation's best, according to U.S. News & World Report's annual Best Hospitals rankings. In addition to Neurology and Neurosurgery, UH Case Medical Center has ranked in 11 other specialties – joining a prestigious group of only 13 hospitals in the country to rank in all 12 methodology-ranked specialties. Some of the other hospitals in this group include Johns Hopkins Hospital, the Mayo Clinic, Massachusetts General Hospital, New York-Presbyterian Hospital and Cedars-Sinai.

24-Hour Rapid Referral

Now connecting your patients to the UH Neurological Institute within 24 hours

Rapid Referral is the fast and convenient way to get connected to our neurological team of experts. Call the UH Rapid Referral line – and your patient is scheduled to see one of our specialists within 24 hours. **Call 216-844-2724 to get an appointment scheduled within 24 hours.**

Physician Advice Line

You're just one phone call away from the finest neurosurgeons, neurologists and specialists in the country. Receive immediate decision-making advice from our team of experts by calling **216-844-1001**.

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Image courtesy of Apple

UH Transfer Referral Center

Our team of transfer liaisons will expedite the process and give you immediate access to our critical care transport teams, board-certified specialists and Beacon Award-winning intensive care unit. The center also provides 24/7 teleconsultation services with nationally recognized experts in stroke, epilepsy (seizures) and other neurological emergencies. Please call **216-844-1111** or **1-800-421-9199** to speak with a transfer referral liaison.